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STRAIN SENSITIVITY OF *TRICHOMONAS VAGINALIS* TO METRONIDAZOLE*

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A previous publication (Kane, McFadzean, Squires, King, and Nicol, 1961) gave the possible reasons for the failure of metronidazole to eradicate *Trichomonas vaginalis* from a small percentage of treated patients. Evidence was obtained (Kane, McFadzean, and Squires, 1961) that a number of failures could be due to defective absorption of the compound. The results of investigating another possibility, namely, resistance of the parasite to the compound, are now presented.

Methods

Patients who apparently failed to respond to the standard course of the drug (200 mg. three times daily for 7 days) were swabbed and a culture was taken into a liver infusion broth of the following composition:

Dehydrated liver infusion (Oxoid)	18 g.
Dextrose	20 g.
Calcium pantothenate (0·5 per cent. solution)	1 ml.
Trypsin digest broth to	1,000 ml.

The medium was adjusted to pH 6 and sterilized at a steam pressure of 5 lb. per sq. in. for 15 minutes. Before use, 10 per cent. v/v inactivated sterile horse serum was added and penicillin, streptomycin, and Mycostatin were also included to eliminate bacterial and mycotic contamination.

Cultures were collected at a number of different centres. On arrival at the laboratory, they were examined microscopically to determine viability, and then incubated at 37°C. for 24 hrs and re-examined. All viable cultures at this time were subcultured and then examined for sensitivity to metronidazole by a serial dilution method, using the medium described above. After 24 hrs' incubation, the deposit in each tube was examined microscopically for evidence of motile trichomonads, and the highest dilution in which no motile organisms were seen was recorded as the minimal inhibitory concentration.

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Results

The results are shown in the Table. Of 42 cultures submitted for sensitivity determination, sixteen were not viable on arrival. Of the other 26 strains, seven were inhibited by 0·25 μg./ml., thirteen by 0·5 μg./ml., and six by 1 μg./ml. No strain grew at a concentration above 1 μg./ml. These sensitivities were within the range obtained against strains maintained before the introduction of metronidazole.

TABLE

RANGE OF SENSITIVITY TO METRONIDAZOLE OF STRAINS OF *T. VAGINALIS* ISOLATED FROM PRIMARY FAILURES

No. of Cultures Taken	No. of Cultures Viable	Sensitivity to Metronidazole (μg.)			Sensitivity of Stock Strain
		0·25	0·05	1	
42	26	7	13	6	0·25–1 μg.

Discussion

Of the various factors involved in the failure of patients to respond to the therapeutic action of metronidazole, the possibility of the occurrence of resistant strains of the protozoon was of prime importance. From the limited *in vitro* studies reported here, it would seem that *no strain* of *T. vaginalis* resistant to metronidazole has so far appeared, and resistance has not therefore been the causative factor in the failure to respond to the drug. Jennison, Stenton, and Watt (1961) have reported failure to induce resistance in *T. vaginalis* to metronidazole *in vitro* and attempts made in these laboratories have also failed.

Summary

Of 42 cultures of *T. vaginalis* taken from patients failing to respond to metronidazole and examined

for sensitivity to the drug, 26 were viable on arrival at the laboratory. The sensitivity to metronidazole of these strains was within the range of 0·25–1 μg./ml., the same sensitivity as stock strains isolated before the introduction of the drug.

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ADDENDUM

Since this work was carried out we have seen a report (Robinson, 1962) that a strain of *Trichomonas vaginalis*, resistant to metronidazole, has been isolated. Unfortunately this strain is not available for investigation.

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Sensibilité des souches de *T. vaginalis* au métronidazole

RÉSUMÉ

Sur 42 souches de *T. vaginalis* prélevées sur des malades qui ne répondaient pas au métronidazole et dont la sensibilité au métronidazole fut examinée, 26 étaient encore en vie en arrivant au laboratoire. La sensibilité de ces souches fut de 0,25 à 1μg./ml., la même que celle des souches isolées avant l'introduction de ce médicament.